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First Synthesis of Tetrapyrrolylporphyrin

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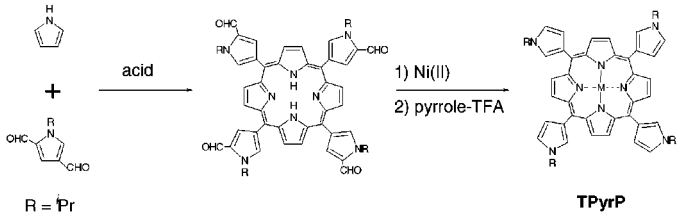
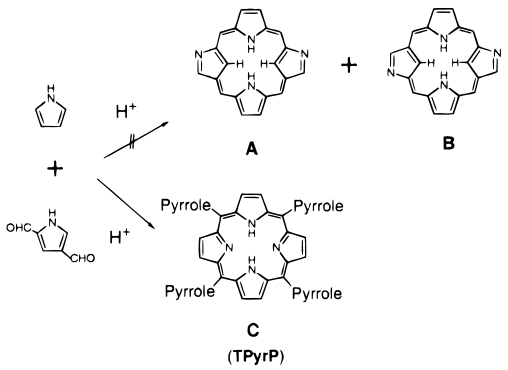
ABSTRACT



***N*-Alkyl-substituted *meso*-tetrapyrrolylporphyrin (TPyrP) and its derivatives were synthesized for the first time via an acid-catalyzed condensation between *N*-alkyl-2,4-diformylpyrrole and unsubstituted pyrrole and a subsequent deformylation reaction. X-ray structural analysis of formyl-substituted TPyrP shows the tilting of meso pyrrole rings ca. 60° to the porphyrin plane. Formyl groups of meso pyrrole rings were removed by treatment with trifluoroacetic acid (TFA) in pyrrole.**

Owing to the facile syntheses and modifications, a variety of meso-substituted tetraarylporphyrins have been synthesized and used in various studies such as modeling of biological processes, catalysts, functional dyes, and so on.[1] Among the *meso*-aryl-substituted compounds, heteroaromatics, like pyridyl or imidazolyl, are of interest because they could serve as building blocks of the metal-coordinated supramolecular assembly.[2] On the other hand, there are few reports about porphyrins with pyrrolyl substituents despite the importantance of the porphyrin framework and its potential application as a molecular wire.[3] During our study to synthesize "doubly N-confused porphyrins",[4] we have examined the acid-catalyzed 1:1 condensation of 2,4-diformylpyrrole and pyrrole to obtain **A** or **B**, expecting that both formyl groups could be involved in the porphyrin macrocycle. Unexpectedly, the products isolated were not "doubly N-confused porphyrins" but *meso*-tetrapyrrolylporphyrins (TPyrPs), **C**, products in which only one of the formyl groups reacted (Scheme 1). Thus, TPyrP contains eight pyrrolyl units in one molecule. In this Letter, we report the synthesis, structural characterization, deformylation reac-

Scheme 1



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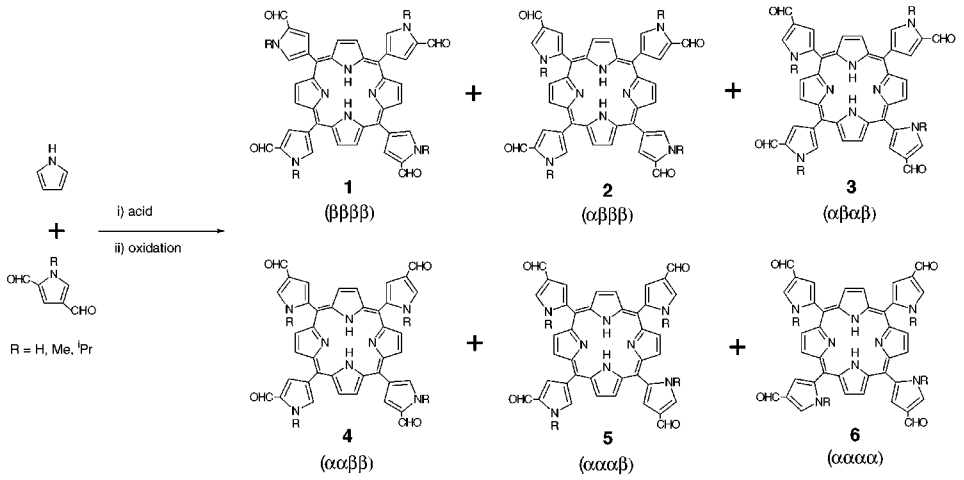
Scheme 2



tion, and unusual optical properties of TPyrP and its derivatives. To the best of our knowledge, this is the first example of porphyrins that have pyrrole rings at all four meso positions.

First, 2,4-diformylpyrrole and unsubstituted pyrrole were reacted in acetic acid at 110 °C for 40 min. After removing the solvent, the brown tar residue was subjected to a silica gel column with 3% MeOH−CH_2Cl_2. Four red colored bands were isolated. They turned out to be formyl-substituted TPyrP, **1**-H, **2**-H, a mixture of **3**-H and **4**-H, and **5**-H from MALDI-TOF and NMR spectra (Scheme 2).[5] Changing the acid to trifluoroacetic acid (TFA) or BF_3·OEt_2 resulted in the formation of insoluble polymers. The *ββββ*-linked product **1**-H was severely insoluble and could not be studied further. α*β*-Mixed formyl TPyrP (**2**-H, **3**-H + **4**-H, and **5**-H), obtained in 5% yields in total (ca. 2:4:1 in ratio), showed two sets of ^{1}H NMR signals with 3:1, 1:1, and 1:3 ratios, respectively. For example, two pyrrolic NH's appeared at 13.01 and 12.94 ppm (3:1) and formyl H's at 9.94 and 10.15 ppm (3:1) with **2**-H in DMF-d_7. Evidence for a mixture of **3**-H and **4**-H (1:1) came from two independent signals of inner NHs at −2.83 and −2.85 ppm.[6] The attempts to purify these products were hampered by their poor solubility. To raise the solubility, *N*-alkyl-substituted 2,4-diformylpyrroles were subjected to the reactions in the next step. When *N*-methyl-2,4-diformylpyrrole was used, the formyl-substituted *N*-methyl-TPyrP, **1**-Me, **2**-Me, and (**3**-Me + **4**-Me) were isolated in 5% yield, and the similarly but α*βββ*-linked product **2**-Me was obtained as a major product. When the more bulky *N*-isopropyl derivative was used, nearly identical amounts of **1**-^{i}Pr and **2**-^{i}Pr were produced in 10% yield, which leads to the conclusion that the diformylpyrrole served as a normal arylaldehyde.[7] In fact, with the standard Lindsey method (BF_3·OEt_2/$CHCl_3$), *ββββ*-linked product **1**-^{i}Pr was obtained in 20% yield but the formation of α*β*-mixed products **2**-^{i}Pr, **3**-^{i}Pr, or **4**-^{i}Pr was not confirmed. The selective formation of **1**-^{i}Pr can be explained by the steric hindrance of *N*-alkyl groups that deactivates the α-formyl group of 2,4-diformylpyrrole.[8] The produced TPyrP **1**-^{i}Pr was therefore derived from the reaction with the remaining *β*-formyl groups and unsubstituted pyrroles.

A single-crystal structure of **1**-^{i}Pr revealed that the meso pyrroles were tilted 57.6 and 61.4° against the mean core plane (Figure 1),[9] which is similar to that of the tetraphenylporphyrin (TPP).[10] The porphyrin plane is almost flat, and the core pyrroles are slightly canted 4.0 and 4.3° in the opposite direction. The deviation from planarity is less than

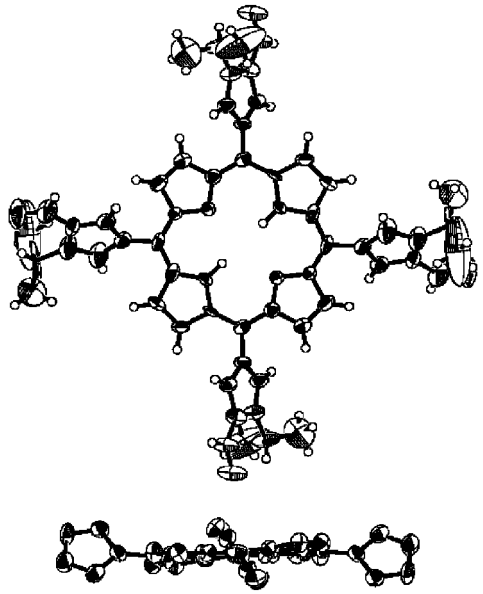


Figure 1. Structure of *N*-isopropyl-TpyrP (**1**-^{i}Pr). Isopropyl and formyl groups are omitted for clarity in the side view.

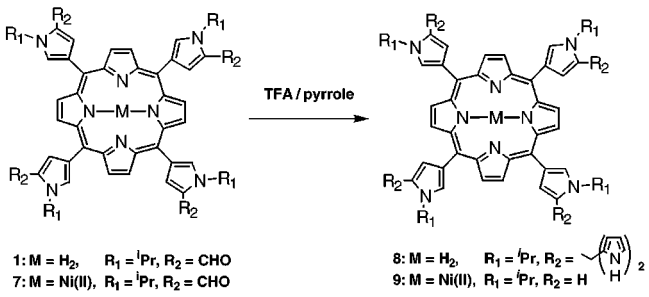
(5) Differentiations between α*βββ* (**2**) and αααβ (**5**) are based on the chemical shifts (ppm) of meso pyrroles: α-linked (7.52, 8.40); *β*-linked (8.20, 8.35). We think the ring current effect differs greatly for α- and *β*-H of an α-linked pyrrole but are similar for a *β*-linked pyrrole.

(6) ^{1}H NMR spectra of selected TPyrP derivative are shown in the Supporting Information.

0.12 Å. Optical absorption spectra show both Soret transition bands and Q-bands around 428.5, 526, 568.5, and 662 nm, respectively. Ni(II) complex (**7**) was also prepared by heating with Ni(II) acetylacetonate in refluxing toluene for 1 h.

The removal of the attached formyl groups succeeded during the synthesis of tripyrromethane derivative **8**, unexpectedly (Scheme 3).[11] When **1**-^{i}Pr was stirred in pyrrole in

Scheme 3



the presence of TFA for 30 min at room temperature, the blue-green colored tripyrromethane derivative **8** was obtained in 90% yield. On the other hand, when Ni complex **7** was treated under the same conditions, the deformylation reaction took place in 3 h, affording the Ni complex of TPyrP, **9**, in 46% yield. Monitoring the reaction by MALDI-TOF-MS suggested that the deformylation of **7** proceeded via tripyrromethane intermediates.

Interestingly, the protonated **8** gives a red-brown colored solution and shows a very large Q-band absorption at 765.5 nm in $CHCl_3$, which is ca. 90 nm bathochromic shifted compared with the free base (Figure 2). Further, the ratio of

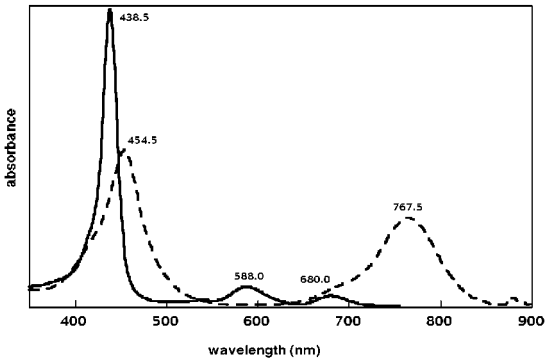


Figure 2. Absorption spectra of tripyromethanederivative **8**: free base (solid line) and protonated **8** (broken line) in CH_2Cl_2.

absorption intensity between Soret and Q-band transition in this protonated porphyrin is 0.56. These values, bathochromic shift and absorption ratio, are in remarkable contrast to those for the protonated TPP, 10 nm and 0.10. Similar trends were also observed for **1**-^{i}Pr, 47 nm and 0.21. At present, we are not sure about the origin of the large absorption change with this 12 pyrrole-substituted porphyrin (16 pyrrolyl units in total), **8**. The large deformation of the porphyrin plane due to the interactions of the pendant pyrrolyl groups and the protonated pyrroles in the core is highly probable.[12]

The reason *meso*-tetrapyrrolylporphyrin (TPyrP) has not been studied is mainly due to the difficulty of synthesis. As the simple formylpyrrole is prone to polymerize, introduction of the second formyl and/or bulky group at pyrrolic-N was an important key for the synthesis of TPyrP. Especially, the remaining second formyl group could be used as a foothold to synthesize various TPyrP derivatives. A modeling study for electron transfer and an application such as photodynamic therapy (PDT)[13] can be contemplated.

Supporting Information Available: Experimental procedures, spectral data for TPyrPs, and X-ray structural details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Selective analytical data for **1**-^{i}Pr: mp > 300 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C) δ (ppm) 9.94 (d, J = 2.0 Hz, 4H, CHO), 9.13 (s, 8H, β-H), 8.00 (s, 4H, pyrrolyl-αH), 7.86 (d, J = 2.0 Hz, 4H, pyrrolyl-βH), 5.84 (sept, J = 6.5 Hz, 4H, CH), 1.80 (d, J = 6.5 Hz, 24H, CH_3); UV/vis ($CHCl_3$) λ_{max}[nm] ($\epsilon \times 10^{-4}$) 428.5 (57), 526.0 (1.4), 568.5 (2.0), 662.0 (0.87); FABMS m/z (% intensity) = 850.6 (84, M^+), 851.7 (100, M^++1); HRMS (FAB) calcd for $C_{52}H_{51}N_8O_4$ [M^+ + H] 851.4033, found 851.4139. Anal. Calcd for $C_{52}H_{51}N_8O_4 \cdot H_2O$: C, 71.87; H, 6.03; N, 12.89. Found: C, 72.26; H, 6.00; N, 12.50. The synthetic details and the spectral data of TPyrPs are shown in the Supporting Information.

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(9) X-ray data of **1**-^{i}Pr (27 °C): violet prismatic, $C_{52}H_{50}N_8O_4$, M_w = 851.02, monoclinic, space group $P2_1/c$ (No. 14), a = 7.308(6) Å, b = 23.279(5) Å, c = 14.447(6) Å, β = 98.12(5)°, V = 2433(2) Å^3, Z = 2, D_{calcd} = 1.161 g/cm^3, R = 0.076, R_w = 0.063, GOF = 2.03. We would like to thank Dr. Takuji Ogawa at Ehime University for initial help with the X-ray structural work.

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(11) Spectral data for **8:** ^{1}H NMR (2% $Et_3N/CDCl_3$, 500 MHz, 27 °C) δ (ppm) 9.14 (br, 8H, dipyrromethane pyrrole-NH), 8.53 (s, 8H, βH), 7.54 (s, 4H, meso pyrrole-H), 6.90 (s, 4H, meso pyrrole-H), 6.78 (d, J = 2.0 Hz, 8H, dipyrromethane pyrrole-H), 6.24 (s, 8H, dipyrromethane pyrrole-H), 6.24 (d, J = 2.0 Hz, dipyrromethane pyrrole-H), 5.89 (s, 4H, dipyrromethane meso-H), 4.64 (sept, J = 6.5 Hz, 4H, isopropyl-CH), 1.53 (d, J = 6.5 Hz, 24H, isopropyl-CH_3), −2.42 (br, 2H, inner NH);UV/vis (CH_2Cl_2) λ_{max}[nm] 438.5, 539.5, 588.0, 680.0; MALDI-TOF-MS m/z = 1315.8 (M^++1). Protonated type of **8**: UV/vis (5% TFA-CH_2Cl_2) λ_{max}[nm] 454.5, 767.5.

(12) NMR spectrum of **8** in 5% TFA/$CDCl_3$ was too broad to get the details about the conformational change upon protonation.

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